

Dakai Liu and Elazar R. Jani

Serial No. 09/046,833

Filed: March 24, 1998

Page 7 [Amendment Under 37 C.F.R. §1.115 (In Response To The
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REMARKS

Reconsideration of this application is respectfully requested.

Claims 75-90 were previously pending in this application. These claims have been canceled in favor of new claims 91-111.

New Claims

New claims 91-111 are all directed to a packaging cell line. Except for some specific changes made for the sake of clarity or to overcome objections, new claims 91-111 correspond in large part to the previously pending claims 75-90.¹ In order to help the Examiner track the correspondence and changes in the new claims, Applicants' attorney has prepared a table below.

<u>New Claim No.</u>	<u>Previously Pending Claim No.</u>	<u>Changes/Remarks</u>
91	75	Same as claim 75 presented 7/29/03
92	76	No change
93	77	"comprise" changed to "comprises"
94	78	No change
95	79	No change
96	80	No change
97	81	No change except for Markush language
98	82	No change
99	83	No change
100	84	No change

¹ In the January 29, 2004 Office Action, the Examiner indicated that "claims 75 and 88-90 will be examined as they appear in the response filed 3/15/02." The above new claims 91 and 109-111 correspond to claims 75 and 88-90 as they were presented in Applicants' July 29, 2003 Amendment Under 37 C.F.R. §1.116, but not examined due to formatting concerns raised by the Examiner.

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101	85	Multiple dependency changed to single dependency (claim 99)
102	85	Same subject matter of claim 101 except dependent from claim 100
103	87	Multiple dependency changed from 3 claims to single dependency (claim 99)
104	87	Same subject matter of claim 103 except dependent from claim 100
105	85-86	Combines subject matter of claims 85 and 86
106	87	Deletion of "of any" and now dependent from claim 103; also change in Markush language
107	87	Same subject matter of claim 106 except dependent from claim 104; also change in Markush language
108	87	Same subject matter of claim 106 & 107 except dependent from claim 105; also change in Markush language
109	88	Same as claim 88 presented 7/29/03 but not examined
110	89	Same as claim 89 presented 7/29/03 but not examined
111	90	Same as claim 90 presented 7/29/03 but not examined

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PAGE 19/31 * RCVD AT 2/12/2007 5:50:43 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-2/3 * DNIS:2738300 * CSID:2125830150 * DURATION (mm:ss):07:36

Dakai Liu and Elazar Rabinovitch

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The anticipation rejection is respectfully traversed.

The present invention is directed to a packaging cell line for propagating a viral vector independent of a helper virus. The viral vector comprises a nucleic acid component and at least two different non-nucleic acid components. One of the non-nucleic acid components has a tropism for the cell line and the other non-nucleic acid component has a tropism for a target cell which is different from the cell line. The nucleic acid component and the non-nucleic acid components are capable of forming a specific complex or complexes, wherein the sequence or sequences for the viral vector nucleic acid component is stably integrated in the genome of the cell line. Furthermore, the sequence or sequences for the non-nucleic acid components of the viral vector are introduced into the packaging cell line by transient expression, episomal expression or stably integrated expression.

Applicants continue to respectfully maintain that neither *Finer et al.* nor *Bodner et al.* anticipate the present invention, particularly where the latter recites that "one of the non-nucleic acid components has a tropism for said cell line and the other non-nucleic acid component has a tropism for a target cell which is different from said cell line."

In further detail, *Finer's '279 Patent* describes using only one particular *env* protein that is selected from a group. This results in only a single tropism, although a variety of different tropisms may be selected. No mention is made of the desirability or utility for having more than one *env* gene in a vector particle. In *Finer's '279 Patent*, there is a reference to *env* proteins or combinations thereof in the claims, but in column 10, lines 19-22, it is revealed that such combination(s) refers to chimeric proteins, i.e., a fusion of portions of two *env* genes to generate a single protein. In no way does *Finer's* disclosure teach or suggest the choice or use of Applicants' claimed tropisms, i.e., one tropism for the cell line and the other tropism for the target cell.

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In the case of Bodner's '746 Patent, it is disclosed in column 19, lines 31-32 that "resultant viral particles contain more than one species of env protein." The context of column 19, lines 10- 46 begins, however, thusly:

Retroviral particles according to the invention may be directed towards a specific cell type by including in the retroviral particles a component, most frequently a polypeptide or carbohydrate, which binds to a cell surface receptor specific for that cell type.

Thus even when there is more than one species of env protein, the resultant viral particle in Bodner's disclosure is still directed towards a specific cell type.

Later sections in Bodner et al. make reference to chimeric molecules, but again, this reference is in the context of an ability to develop targeting to a specific cell type. Bodner et al. state in column 20, lines 14-16:

To accomplish this, the gene coding for the ligand can be functionally combined with the sequences coding for a membrane-associated domain.

In contrast to Bodner et al., the present invention comprises two tropisms and as such, it is not directed to a specific cell type. Indeed, the present invention and packaging cell line is directed to at least two different cell types:

- a) the packaging cell line; and
- b) a target cell type that is different from the packaging cell line.

The Bodner references makes no reference as to the utility or the desirability for a tropism other than the target cell. Thus, the dual tropism recited in the present claims is altogether lacking in Bodner et al.

In summary, the cited Finer and Bodner patents clearly lack an identity of material elements with Applicants' claimed invention, namely, the instantly claimed tropism for the cell line and a tropism for the target cell.

In view of the clear lack of identity between the cited patents and their present claimed invention, Applicants respectfully request reconsideration and withdrawal of the anticipation rejection.

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Commonality of Ownership

Applicants again acknowledge the Examiner's comments on page 4 of the January 29, 2004 Office Action regarding common ownership of the claims and invention. As indicated in earlier response(s), Applicants confirm that the subject matter of the various claims was commonly owned at the time any inventions covered therein was made.

The First Rejection Under 35 U.S.C. §103(a)

Claims 83 and 85 stand rejected under 35 U.S.C. §103(a) as being unpatentable over *Finer et al.* or *Bodner et al.*, either in view of *Respass et al.* In the Office Action (pages 4-6) it is stated:

Applicants claim a packaging cell comprising a viral vector which encodes an antisense RNA targeted against a mRNA coding for an undesirable protein in a target cell.

Fine et al. and *Bodner et al.* are cited as in the above 35 USC 102(e) rejection of claims 75-82 and 88-90. Neither *Finer et al.* nor *Bodner et al.* teach expression of antisense sequences by viral vectors.

Respass et al. (U.S. Patent 6,013,517, issued 1/11/00, effective filing date 5/9/94, see whole document, particularly Columns 14-15, Claims 1, 8 and 11) recites the generation of packaging cell lines capable of generating retroviral vectors which are capable of expressing antisense RNAs complementary to undesirable mRNAs (i.e. mRNAs coding for cellular proteins required for cell growth in cancer cells) produced by target cells.

The ordinary skilled artisan, seeking to generate retroviral vector packaging cells capable of generating retroviral vectors capable of expressing an antisense sequence directed against the mRNA from an undesirable gene in a target cell, would have been motivated to combine the teachings of *Finer et al.* or *Bodner et al.* on the generation of retroviral packaging cells with the characteristics of claims 75-82 and 88-90 with the teachings of *Respass et al.* on the packaging cells which generate retroviral vectors capable of expressing antisense sequences targeted against mRNAs from undesirable genes in target cells because the expression of antisense sequences targeted against

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undesirable genes in target cells has been a well known techniques to inhibit the growth of undesirable target cells or inhibit virus replication, etc. It would have been obvious for the ordinary skilled artisan to do this because use of viral (retroviral) vectors to deliver antisense sequences to target cells, in the context of treatment of diseases, was well known in the art (see Respass et al.) and was a standard use of retroviral vectors. Given the teachings of the cited prior art and the level of skill the ordinary skilled artisan at the time of applicants' invention, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

The first obviousness rejection is respectfully traversed.

As indicated in the anticipation rejection above, neither Finer et al. nor Bodner et al. disclose the instantly claimed packaging cell line in two tropisms are present. Thus, even the addition of the Respass '517 Patent does not render Applicants' claimed invention obvious.

Furthermore, there is no disclosure or suggestion in any of the cited primary documents or the secondary document to combine the respective disclosures as set forth in the instant Office Action. Armed with the combination of cited documents, a person of ordinary skill in the art would not have arrived at Applicants' claimed packaging cell line in which two tropisms are materially recited, one for the cell line and the other for the target cell.

In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the first obviousness rejection.

The Second Rejection Under 35 U.S.C. §103(a)

Claim 84 stands rejected under 35 U.S.C. §103(a) as being unpatentable over Finer et al. in view of Bujard et al. In the Office Action (pages 6-7) it is stated:

Applicants claim a viral packaging cell line wherein the viral vector produced expresses a polypeptide of interest and an antisense RNA in a target cell.

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instant Office Action. A person of ordinary skill in the art would not have arrived at Applicants' claimed packaging cell line in which two tropisms are materially recited, one for the cell line and the other for the target cell, from a combined reading of *Finer et al.* and *Bujard et al.*

In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the second rejection under §103(a).

The Third Rejection Under 35 U.S.C. §103(a)

Claims 83, 85, 86-87 stand rejected under 35 U.S.C. §103(a) as being unpatentable over *Finer et al.* in view of *Dietz et al.* In the Office Action (pages 7-8) it is stated:

Applicants claim a packaging cell line comprising a viral vector which encodes an antisense RNA targeted against a mRNA coding for an undesirable protein in a target cell and wherein the antisense RNA can be a part of a chimeric RNA molecule that comprises sequences from small nuclear RNAs (for example, U1 snRNA).

Finer et al. is as cited in the above 35 USC 102(e) rejection of claims 75-82 and 88-90. *Finer et al.* does not teach expression of antisense sequences by viral vectors.

Dietz (U.S. Patent 5,814,500, issued 9/29/98, filed 10/31/96, see whole document, particularly Columns 2-3, 8 and Claims 1-11) recites the use of retroviral vectors to express antisense sequences targeted against undesirable target genes and wherein the antisense RNA is part of a chimeric RNA molecule that comprises sequences from snRNAs (such as U1 snRNA).

The ordinary skilled artisan, seeking to develop packaging cell lines capable of generating retroviral vectors capable of expressing an antisense sequence or a chimeric antisense RNA molecule, would have been motivated to combine the teachings of *Finer et al.* on the generation of retroviral packaging cell lines with the characteristics of claims 75-82 and 88-90 with the teachings of *Dietz* concerning the use of retroviral vectors to express chimeric antisense sequences targeted against undesirable genes in target cells because the expression of antisense sequences targeted against undesirable genes was a well known technique in molecule biology and use of retroviral vectors to deliver chimeric RNAs to target cells was likewise known

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(Dietz). It would have been obvious for the ordinary skilled artisan to do this because delivery and expression of antisense sequences targeted against undesirable genes had been a well known (for almost two decades) technique in molecular biology. It would further have been obvious for the ordinary skilled artisan to select chimeric RNAs encoding antisense sequences and snRNAs because Dietz teaches that said chimeric RNAs make superior delivery vehicles for delivering the antisense sequences to the target cells. Given the teachings of the cited prior art and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

The third obviousness rejection is respectfully traversed.

As also indicated above, Finer's cited U.S. patent does not disclose the instantly claimed packaging cell line wherein one of the non-nucleic acid components has a tropism for a cell line and the other non-nucleic acid component has a tropism for a target cell which is different from the cell line. Lacking the two tropisms of the presently claimed invention, Finer's disclosure cannot be supplemented by the Dietz '500 Patent to render the instant claims obvious. To stated in another way, a person of ordinary skill in the art would not have arrived at Applicants' instantly claimed packaging cell line, merely from a combined reading of Finer et al. and Dietz et al.

In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the third rejection under §103(a).

The Rejection Under 35 U.S.C. §112

Claim 77 and 88-90 stand rejected under 35 U.S.C. §112, second paragraph for indefiniteness. In the Office Action (page 9) it is stated:

Claim 77 is vague in that the tense of the word "comprise" should be singular (comprises) not plural.

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Claim 87 is vague in that it refers to "The packaging cell line of any of claim 86..." because there is only one claim 86.

Claims 88-90 are vague in the recitation of the phrase "virus that is native to" the cell line or target cell. It is unclear if this phrase means that the virus naturally infects and replicates within the cell or that the virus can infect the cell but not replicate in the cell, or that the virus genome is present in the cell but it is not replicated, etc.

The indefiniteness rejection is respectfully traversed.

As indicated above, all three matters raised in this rejection have been obviated by the presentation of the new claims, particularly, claim 93 ("comprise" changed to "comprises"), claim 106 (deletion of "of any"), and claims 109-111 (deletion of "native" in favor of "tropism"). It is believed that the language in new claims 93, 106 and 109-111 clarifies the claimed subject matter.

In view of the above amendment and foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the indefiniteness rejection.

Favorable action on this application is respectfully urged.

* * * * *

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SUMMARY AND CONCLUSIONS

Claims 91-111 have been added in place of previously pending and now canceled claims 75-90.

The claim fee for adding new claims 91-111 is \$25 based upon the presentation of one additional claim above the 20 claims previously paid for (1 X \$25 = \$25). The Patent and Trademark Office is hereby authorized to charge the requisite \$25 claim fee to Deposit Account No. 05-1135. No other fee or fees are believed to be due in connection with this Amendment or the accompanying filings. If any other fee or fees are due, however, for either this response or the accompanying filings, The Patent and Trademark is authorized to charge the amount of any such fee(s) to Deposit Account No. 05-1135, and to credit any overpayment thereto.

Applicants respectfully submit that all of the instant claims are in allowable condition. Should it be deemed helpful or necessary, the Examiner is respectfully invited to telephone the undersigned at (212) 583-0100 to discuss the subject application.

Respectfully submitted,



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Dakai Liu & Elazar Rabbani, Serial No. 09/046,833 (Filed March 24, 1998)
Exhibit B (To Communication (Directed To August 19, 2005 Petition & Amendment
Under 37 C.F.R. §1.115) -- February 12, 2007]

EXHIBIT B

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Transaction History

Date	Transaction Description
10-24-2005	Correspondence Address Change
08-11-2004	Mail Abandonment for Failure to Respond to Office Action
08-09-2004	Abandonment for Failure to Respond to Office Action
04-29-2004	New or Additional Drawing Filed
03-17-2004	Information Disclosure Statement (IDS) Filed
01-29-2004	Mail Non-Final Rejection
01-26-2004	Non-Final Rejection
11-20-2003	Reference capture on IDS
10-30-2003	Information Disclosure Statement (IDS) Filed
11-18-2003	Date Forwarded to Examiner
10-24-2003	Request for Continued Examination (RCE)
11-18-2003	DISPOSAL FOR A RCE/CPA/129 (express abandonment if CPA)
10-24-2003	Information Disclosure Statement (IDS) Filed
10-24-2003	Affidavit(s) (Rule 131 or 132) or Exhibit(s) Received
10-24-2003	New or Additional Drawing Filed
10-24-2003	Workflow - Request for RCE - Begin
10-08-2003	Mail Advisory Action (PTOL - 303)
10-07-2003	Advisory Action (PTOL-303)
09-29-2003	Date Forwarded to Examiner
07-29-2003	Amendment/Argument after Notice of Appeal
07-29-2003	Notice of Appeal Filed
07-29-2003	Terminal Disclaimer Filed
09-30-2003	Mail Notice of Rescinded Abandonment
09-29-2003	Notice of Rescinded Abandonment in TCs
09-25-2003	Petition to Revive Application - Granted
07-29-2003	Petition Entered
02-11-2003	Mail Abandonment for Failure to Respond to Office Action
02-10-2003	Abandonment for Failure to Respond to Office Action
06-26-2002	Mail Final Rejection (PTOL - 326)
06-26-2002	X-Post-Legal Complete Rejection
06-26-2002	Final Rejection
04-29-2002	X-Pre-Legal Complete Amended Case
04-29-2002	Date Forwarded to Examiner
03-15-2002	Response after Non-Final Action
03-15-2002	Terminal Disclaimer Filed
04-30-2002	Mail Notice of Rescinded Abandonment
04-29-2002	Notice of Rescinded Abandonment in TCs
04-24-2002	Petition to Revive Application - Granted
03-15-2002	Petition Entered
07-09-2001	Mail Abandonment for Failure to Respond to Office Action
07-09-2001	Abandonment for Failure to Respond to Office Action
12-15-2000	Mail Non-Final Rejection
12-15-2000	Non-Final Rejection
12-06-2000	Date Forwarded to Examiner
11-30-2000	Request for Continued Examination (RCE)
11-30-2000	Mail Express Abandonment (During Examination)
11-30-2000	Express Abandonment (during Examination)

11-30-2000 Request for Extension of Time - Granted
 11-30-2000 Workflow - Request for RCE - Begin
 07-11-2000 Mail Advisory Action (PTOL - 303)
 07-10-2000 Advisory Action (PTOL-303)
 07-10-2000 Withdraw Publication/Pre-Exam Abandon
 05-26-2000 Affidavit(s) (Rule 131 or 132) or Exhibit(s) Received
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 01-05-2000 Mail Abandonment for Failure to Respond to Office Action
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 05-26-1999 Mail Final Rejection (PTOL - 326)
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 03-10-1999 Response after Non-Final Action
 03-10-1999 Request for Extension of Time - Granted
 06-05-1998 Mail Non-Final Rejection
 06-05-1998 Non-Final Rejection
 05-21-1998 Case Docketed to Examiner in GAU
 03-24-1998 Preliminary Amendment
 04-15-1998 Case Docketed to Examiner in GAU
 04-09-1998 Application Dispatched from OIPE
 04-04-1998 IFW Scan & PACR Auto Security Review
 03-26-1998 Initial Exam Team nn

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